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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/505,200	04/18/2005	Roberto D'Alessio	17722 (PC27004)	5147

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EXAMINER

HAVLIN, ROBERT H

ART UNIT	PAPER NUMBER
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1626

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02/26/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/505,200	Applicant(s) D'ALESSIO ET AL.	
	Examiner ROBERT HAVLIN	Art Unit 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 November 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13 and 21-32 is/are pending in the application.
- 4a) Of the above claim(s) 1-12, 23-26 and 28-32 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 13, 21 and 27 is/are rejected.
- 7) ☒ Claim(s) 22 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the claims: Claims 1-13, 21-32 are currently pending.

Priority: This application is a 371 of PCT/EP03/01594, filed 02/18/2003, which claims benefit of US Provisional Application No. 60/357,918, filed 02/19/2002.

RCE: A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/26/08 has been entered.

RESPONSE TO APPLICANT ARGUMENTS

1. Claims 13, 21, and 27 were rejected under 35 USC 112 1st paragraph as failing to comply with the written description requirement. Based on applicant's arguments, the original claims as filed, and the content of exhibit A filed on 11/26/2008, **this rejection is withdrawn.**

NEW CLAIM REJECTIONS

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 13, 21, and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter

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which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

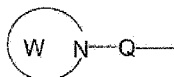
The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in *Wands* states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

(1) *The nature of the invention and (2) the breadth of the claims:*

The claim scope of R2 vastly exceeds the disclosure and the abilities of one of ordinary skill in the art to synthesize organic compounds without undue experimentation. For example the specification does not enable a genus of compounds have R2 as a 12 membered monocyclic ring with 3 nitrogens substituted with 12 R3 groups selected from NR'SO₂NR'R'' where R' is oxadiazole, R'' is triazole, etc.

R₂ is, each independently, hydrogen, alkyl, 5 to 12 membered mono- or bi-cyclic ring having from 0 to 3 heteroatoms selected from S, O and N, optionally substituted with one or more -(CH₂)_q-R₃ groups; or R₂ is a group of formula



W is a 3 to 7 membered ring having one N heteroatom directly linked to Q and from 0 to 2 additional heteroatoms selected from the group consisting of S, SO, SO₂, O, N and NR'; with the proviso that when L is H, R₂ is not present;

Q is a divalent group selected from CO, SO₂ and (CH₂)_n, wherein n is 0, 1, or 2;

q is, each independently, 0 or an integer from 1 to 3;

R₃ is selected, each independently, from the group consisting of alky, halogen, CF₃, OCF₃, NO₂, CN, C(=NR')NR'R'', OR', SR', OCOR', OCONR'R'', COCF₃, COR', CO₂R', CONR'R'', SO₂R', SO₂NR'R'', NR'R'', NR'COR', NR'COOR', NR'CONR'R'', NR'SO₂R', NR'SO₂NR'R'';

R' and R'' are selected, each independently, from the group consisting of hydrogen, hydroxy, alkyl, hydroxyalkyl, alkenyl, alkynyl, aryl, arylalkyl, heterocyclyl or heterocyclyl-alkyl;

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

The state of the prior art is exemplified by March's as referred to in the prior office action. As indicated by March, for example, the hydrazine reaction can lead to unpredictable side reactions and unwanted products depending on the particular stereochemistry, reaction conditions, etc.

(5) The relative skill of those in the art:

Although the level of skill in the art of synthetic chemistry is very high, there is a large amount of unpredictability in the nature of chemical reactions such that functional groups can interfere with the general synthetic schemes provided. Furthermore, the synthesis of particular positional substitutions can in some cases be very difficult and perhaps impossible with generic synthetic methods.

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(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for a limited number of generic synthetic routes.

However, the specification does not provide sufficient number of species or blazemarks with respect to the variable R2.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to R2 and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

The minimal guidance and evidence in the disclosure of the specification regarding the genus, subgenus, working examples, assays, along with the fact that the breadth of the instant claim covers an extremely broad genus comprising an immense number of species would be unpredictable and lead a skilled artisan to perform undue experimentation to practice the full scope of the claimed subject matter.

Without a more detailed description of the means of arriving at the extremely diverse compounds encompassed by the genus, one of ordinary skill in the art would not recognize that a high percentage of species which fall within the genus, in fact, are capable of being synthesized, not to mention have any asserted utility.

Applicant argues that the variable R2 has sufficient 112 support because the scheme on page 17 of the specification teaches a generic method of making the claimed products with commercially available isothiocyanates. To support this assertion, applicant provided a list of allegedly commercially available isothiocyanates. However, the cited generic scheme III would pose numerous problems in utilizing the cited compounds because of the subsequent steps. For example, March (March's Advanced Organic Chemistry, 5th ed. (2001)) on pages 1192-93 teaches that hydrazine can react with ketones and aldehydes to produce unwanted products other than the ring formation desired. Similarly, the aminolysis step would also cause unwanted side reactions depending on the R2-NCS used. In addition, the scope of the compounds listed in exhibit A are primarily directed to substituted phenyl compounds and do not include the diversity of structures contemplated by the claims. For example there are no 12 membered monocyclic hetero rings with 3 heteroatoms.

Therefore, one of ordinary skill in the art would not readily understand how to make the entire scope of R2 as currently claimed. As mentioned in the prior office action and in the interview of 1/16/08, the scope of R2 supported by the original disclosure includes phenylamino and possibly more depending on the problems one of ordinary skill in the art might encounter with the disclosed methods of making the compounds as discussed above. Therefore, one of ordinary skill in the art would not appreciate that applicants possessed the entire scope of the claims.

7. Claim 13 is rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for "isomers" or "carriers"

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thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

In In re Wands, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. The nature of the invention,
2. The state of the prior art,
3. The predictability or lack thereof in the art,
4. The amount of direction or guidance present,
5. The presence or absence of working examples,
6. The breadth of the claims,
7. The quantity of experimentation needed, and
8. The level of the skill in the art.

The nature of the invention

The nature of the invention is compounds of Formula Ig and isomers or carriers thereof.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that an isomer is any compound having the same composition, including constitutional isomers, which are compounds whose atoms are connected differently and stereoisomers. Constitutional isomers can contain different functional groups in varying positions. Carriers thereof has many meanings to one of ordinary skill in the art and could encompass prodrugs, etc.

The amount of direction or guidance present and the presence or absence of working examples

The only direction or guidance present in the instant specification is for the compounds of Formual I. There is no direction or guidance at to what type of isomers or carriers are included in the claims.

There is no data present in the instant specification for the preparation of any type of isomer, such as constitutional isomers or any prodrug forms.

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The breadth of the claims

The instant breadth of the rejected claims is broader than the disclosure, specifically, the instant claims include any isomer, i.e. any compound with the same number of each atom or prodrug (having a cleavable group to yield the active drug in vivo).

The quantity or experimentation needed and the level of skill in the art

While the level of the skill in the pharmaceutical arts is high, it would require undue experimentation of one of ordinary skill in the art to prepare any isomer as instantly claimed since an isomer of the compounds need only have the same composition of atoms, not necessarily the same order of atoms and can have varying functional groups in varying positions. Therefore, the claims lack enablement for isomers. In addition, it is not clear how one of ordinary skill in the art would modify Formula Ig to arrive at a "carrier" or prodrug form of the compound and finding such a form would require undue experimentation. Therefore, the claim lack enablement for "carriers".

This rejection can be overcome by deleting all instances of "isomers" and "carriers".

Objections

Claims 22 is objected to for being dependent on a rejected base claim.

Conclusion

The claims are not in condition for allowance.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT HAVLIN whose telephone number is (571)272-9066. The examiner can normally be reached on Mon. - Fri., 7:30am-5pm EST.

If attempts to reach the examiner by telephone are unsuccessful the examiner's supervisor, Joe McKane can be reached at (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert Havlin/
Examiner, Art Unit 1626

/Rebecca L Anderson/
Primary Examiner, Art Unit 1626